of antimicrobial activity of sublancin embraces many human pathogens, such as strains of *Bacillus*, *Enterococcus*, *Lactococcus*, *Listeria*, and *Staphylococcus*; and therefore includes *Bacillus anthrasis*, which is the causative agent of the often-fatal disease called anthrax.

REMARKS

Claims 1-23 are pending in this application. Claims 9-14 have been withdrawn from consideration by the Examiner. In this amendment, Claims 4, 16, and 9-14 have been cancelled. Additionally, it was noted that two Claim 6's were included in the application. For ease of understanding, both of these claims were cancelled and replaced with new Claims 24 and 25. New Claims 24 and 25 are duplicates of the Claim 6's. Claims 1, 7, 15, and 20 have been amended. No new matter has been added.

The Examiner has withdrawn Claims 9-14 from consideration as these claims were not elected for prosecution. Claims 9-14 have been cancelled without prejudice in this amendment.

The Examiner has objected to the form of the Information Disclosure Statement ("IDS"). In particular, the Examiner has objected to reference AM. It was noted that the IDS failed to disclose the year of publication for the reference. Attached to this Response is a new PTO Form-1449 containing the Examiner's changes and the publication date (1997). It is requested that the objection be withdrawn and that reference AM be considered.

The Examiner has objected to the specification because page 1, section 0002, line 2 recites an application number. The specification has been amended to remove

the reference to application number 09/462,478. It is requested that the objection be withdrawn.

Claim 16 has been objected to because it is missing the word "of" between the "1-37" and "SEQ" terms. Claim 16 has been cancelled. Therefore, it is requested that the objection be withdrawn.

The Examiner has rejected Claims 1-8, 15, and 17-23 under 35 U.S.C. 112, first paragraph, as not enabled. The Examiner, however, has conceded that the specification adequately enables SEQ ID No. 2. Therefore, Claims 1 and 15 have been amended to limit their scope to SEQ ID No. 2. Because Claims 2-8 and 17-23 are dependent upon these claims, no amendment to Claims 2-8 and 17-23 is required. It is requested that the rejection be withdrawn in light of these amendments.

Additionally, it has been noted that the Examiner stated that in regards to Claims 20-21, Paik showed no activity of sublancin 168 against Gram-negative bacteria and that the specification offered no information to counter this finding. 35 U.S.C. 112 states that

> "[the] specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Applicant submits that in light of the requirements of 35 U.S.C. 112, first paragraph, Paik is <u>irrelevant</u> to an enablement rejection. The present application contains an adequate written description that would enable one of ordinary skill to make and use the invention. It is submitted that Paik offers nothing to contradict the teachings of the present application. However, in the interest of advancing prosecution, Claim 20

has been amended to recite that gram positive bacteria are being treated. As Claim 21 depends upon Claim 20, it is submitted that no amendment is required for Claim 21. In light of the amendment, it is requested that the rejection be withdrawn.

Claim 23 has also been rejected under 35 U.S.C. 112, first paragraph, as not adequately described in the specification. The Examiner has questioned whether the specification is sufficiently enabling for the decontamination of an area. It is submitted that this rejection is not well taken.

MPEP section 2164.05(a) states that the "specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." It is submitted that any person who specializes in the decontamination of areas would know how to decontaminate an area, as well as how to wear a protective suit. Therefore, it is submitted that it is unnecessary under the MPEP to include this information in the specification.

Additionally, it appears that the Examiner has questioned the disclosure of the specification in regards to treating areas contaminated with anthrax. It is submitted that the use of *B. cereus* T spores (as was done in the specification) is an art-recognized model for testing activity against anthrax. Attached to this Response is an internet citation (see: http://nano.med.umich.edu/anti_infectives.html) in which it is stated that *B. cereus* can be used as a substitute for anthrax. Therefore, it is submitted that the specification is enabling for anthrax as well. It is requested that the rejection be withdrawn in light of the above facts.

Claims 1-8 and 15-22 have been rejected under 35 U.S.C. 103(a) as obvious in view of Paik and Olsen. The Examiner has taken the position that Paik teaches that the

production of the antimicrobial peptide sublancin-168 and the activity of the peptide against a variety of different bacteria that are either Gram positive or negative. However, the Examiner noted that Paik does not teach the addition of a His-tag to the peptide for purification. The Examiner has cited Olsen to teach the addition of a His-tag for purification purposes, but noted that Olsen is silent as to sublancin. The Examiner has advanced that it would have been obvious to one of ordinary skill to combine these references to produce the claimed subject matter.

It is submitted that this rejection is not well taken. As the Examiner has observed, page 6, lines 17-22, of the present specification indicate that attempts to label other lantibiotics were not successful. In response to the Examiner's statement that no further information to support this position was given, the following is submitted.

It is submitted that sublancin could not have been expected to be labeled with a His-tag. This is because it was believed in the art that the changes to the C-terminal end of a lantibiotic (from the labeling) would result in the inactivity of the lantibiotic. This belief was supported by the experiments discussed in the specification regarding subtilin. In these experiments with subtilin, the C-terminal end of the precursor peptide had been changed by the labeling of the subtilin. Additionally, it is submitted that the paper by Chakicherla & Hansen (J. Biol. Chem., vol 270, p2353,1995) provides a published example of how subtilin cannot be properly biosynthesized if its C-terminal end had been changed. Additionally, several experiments appear in a University of Maryland Ph.D. Thesis (Rodriguez, Univ of MD) in which the experimenter attempted to add His-tags, etc., to subtilin and failed to obtain an operable His-tag labeled subtilin.

Applicant is in the process of obtaining a copy of this thesis and will forward it to the Examiner in the form of a Supplement to this Response shortly.

Because of these results, it was believed that lantibiotics, in general, would not tolerate changes to their C-termini. It was also believed that the C-terminus was crucial in the recognition of the lantibiotics and their ability to be processed by the post-translational processing machinery. The fact that sublancin was synthesized in the present invention with full activity, despite the His-tag being attached, was a surprise. Therefore, it is submitted that it would not have been obvious in light of the teachings of the Paik and the Olsen references to produce a lantibiotic with a His-tag as it was art recognized that such a lantibiotic was not be possible. It is requested that the rejection be withdrawn.

Claims 1-8 and 15-22 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of Claims 1-9, 11-14, and 30 of copending application No. 09/462,478. Applicant in the process of obtaining an executed Terminal Disclaimer. Attached to this Response is an unsigned Terminal Disclaimer for the Examiner's consideration. It is requested that the rejection be withdrawn upon receipt of the signed Terminal Disclaimer which will be filed shortly as a Supplement to this Response.

In the event this paper is not timely filed, Applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to Applicant's Deposit Account No. 01-2300. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300, referring to client-matter number 108172-00058.

Respectfully submitted,

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Attachments: PTO Form 1449
Internet Citation
Marked Up Copy of the Specification
Marked Up Copy of the Claims
Unexecuted Terminal Disclaimer

MARKED UP COPY OF THE SPECIFICATION

[0002] Sublancin 168 was originally discovered in the laboratory of this Inventor [(U.S. Ser. No. 09/462,478)]. The structure of sublancin and its chemical, physical, and biological properties have been published (3). Properties of sublancin that are relevant to this invention are that it is highly active toward inhibition of outgrowth of spores of *Bacillus*, and that it is extremely stable and resistant to both chemical and proteolytic degradation. The natural spectrum of antimicrobial activity of sublancin embraces many human pathogens, such as strains of *Bacillus*, *Enterococcus*, *Lactococcus*, *Listeria*, [*and*] and *Staphylococcus*; and therefore includes *Bacillus anthrasis*, which is the causative agent of the often-fatal disease called anthrax.

MARKED UP COPY OF THE CLAIMS

1. (Amended) An affinity-tag labeled sublancin peptide comprising a chimeric polypeptide comprising a sublancin peptide, an amino acid spacer attached to the C-terminus of the sublancin peptide, and an affinity tag attached to the spacer, wherein the sublancin peptide comprises amino acid residues 1-37 of SEQ ID No. 2.

7. (Amended) The affinity-tag labeled sublancin peptide of claim [6] 25, wherein the affinity tag comprises from 2-6 histidine residues.

15. (Amended) A method of purifying an affinity-tag labeled sublancin peptide from a solution, the peptide comprising a sublancin peptide, an amino acid spacer attached to the C-terminus of the sublancin peptide, and an affinity tag attached to the spacer, and wherein the method comprises contacting the peptide with a solid support having an affinity for the affinity tag, and wherein the sublancin peptide comprises amino acid residues 1-37 of SEQ ID No. 2.

20. (Amended) A method for decontaminating a gram positive bacterial spore-infected area comprising treating the infected area with a spore-inhibiting effective amount of a peptide according to claim 1.